UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,831	09/04/2001	Susanne Klumpp	MERCK 2296	4120

23599 7590 06/30/2003

MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER
NASHED, NASHAAT T

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
09/914,831	Klumpp et al.
Examiner	**Art Unit**
Nashaat T. Nashed	1652

Office Action Summary

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Sep 4, 2001*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above, claim(s) *7* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-6 and 8-11* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Sep 4, 2001* is/are a) ☐ accepted or b) ☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☒ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *4*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

The application has been amended as requested in the communication filed September 4, 2001. Accordingly, claims 8, 10, and 11 have been amended.

Claims 1-11 are pending.

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Group I: Claims 1-6, and 8-11 drawn to human histidine phosphatase, nucleic acid encoding said phosphatase, antibodies, and pharmaceutical composition comprising said phosphatase, classified in class 435, subclass 195.

Group II: Claims 1-4, 6-8, 10, and 11 drawn to rabbit histidine phosphatase, nucleic acid encoding said phosphatase, antibodies, and pharmaceutical composition comprising said phosphatase, classified in class 435, subclass 195.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The special technical features of the inventions of Groups I and II are independent chemical compound having different structure, the human and rabbit histidine phosphatase, respectively..

During a telephone conversation with John Sopp on May 6, 2003 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-6, and 9-11. Affirmation of this election must be made by applicant in replying to this Office action. Claims 7 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With

Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Specifically, there are several amino acid sequences on page 11, lines 16-26 which are not identified with a sequence identification numbers. Claims 2-5 and 9 contains nucleic or amino acid sequences which are not identified by a sequence identification number. Applicants must perfect their compliance with the sequence rule.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

New formal drawings are required in this application because some of the drawing are of poor quality, see for example Figure 2 does not show any of result described in the Figure description; see also Figure 4. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim 6 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 6 is dependent on claim 3 which is limited to histidine phosphatase, presumably, comprising SEQ ID NO: 4. It expands the scope of claim 3 to encompass all amino acid sequences having sequence homology of 64-99% to SEQ ID NO: 4.

35 U.S.C. § 101 reads as follows:
"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 1-7, 9 and 11 are rejected under 35 U.S.C. § 101 because the claimed invention is directed toward non-statutory subject matter.

In the absence of the hand of man, naturally occurring proteins and/or nucleic acids are considered non-statutory subject matter. *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). This rejection may be overcome by amending the claims to contain wording such as "An isolated and purified protein or nucleic acid".

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6, 8, 10 and 11 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to the rabbit histidine protein phosphatase (HPP) purified by the scheme shown in figure 1, the human HPP of SEQ ID NO: 2, nucleic acid, antibody and composition of HPP thereof. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to any mammalian HPP. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses any mammalian HPP purified having molecular weight of 13-15 kDa measured by any method and purified by a method comprising any anion exchange column, any affinity column which include sepharose or any other resin modified in any way such as hydrophobic interaction columns, DNA columns and/or phosphocellulose columns. The specification provides guidance and examples in the form of an assay to purify HPP from rabbit, clone the rabbit enzyme, and identify the human homolog of HPP by sequence homology to the rabbit enzyme. While molecular biological techniques and genetic manipulation to clone and express specific known proteins are known in the prior art and the skill of the artisan are well developed, knowledge regarding purification method of all mammalian HPP, their sequence homology to the disclosed rabbit and human HPP, the mammalian HPP that are amenable to the purification method taught in the application to purify the rabbit HPP, and a disease which can be treated with the pharmaceutical composition of claim 10 is lacking. The application teaches only the purification of the rabbit enzyme. Thus, searching for a mammalian HPP which can be purified by a method including any affinity column and having a molecular weight between 13 and 15 kDa measured by any method, nucleic acid encoding said HPP, and antibody specific against said HPP as well as identifying a disease which can be treated with said HPP is well outside the realm of routine experimentation and predictability in the art of success is extremely low. The amount of experimentation requires to purify a mammalian HPP, cloning the nucleic acid encoding said HPP, and expressing the HPP in a host cell is enormous. Since routine

experimentation in the art does not include screening large number of genomic, and cDNA libraries where the expectation of obtaining the desired HPP is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the mammalian source of an HPP that can be purified with the described method for the rabbit enzyme, the nucleic acid sequence homology among all nucleic acid encoding mammalian HPP, and the disease which can be treated with the pharmaceutical composition comprising HPP. Without such a guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 and 8-11 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

(a) the phrases "biological activity", "histidine phosphatase", "molecular weight of 13.000-15.000" and "affinity chromatography" in claims 1, 5, and 6, and the nucleic and amino acid sequences in claims 2, 3, 5, and 9 render the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Histidine phosphatase is an enzymatic activity which involve the hydrolysis of a phosphate group of the amino acid histidine. The specification does not teach such an activity. It teaches a histidine protein phosphatase activity in which the histidine is a part of a peptide chain and one of the aromatic ring nitrogen is phosphorylated. The histidine protein phosphatase activity is an intrinsic property of the protein of SEQ ID NO: 2, and therefor its a chemical activity, and not a biological activity. A "molecular weight of 13.000-15.000", presumably, in Da units, corresponds to the atomic weight of ^{13}C and ^{15}N, respectively. A molecular weight must be accompanied with a unit such as atomic unit or Da. Since the applicant probably is referring to a protein of the size of SEQ ID NO: 2, it is assumed that the molecular weight is 13,000-15,000 Da. Even with this assumption in mind, the phrase remains indefinite because the method of determining the molecular weigh is not defined. Since determining the molecular weight of a given protein by different methods may produce different results, the method used to produce the molecular weight must be stated in the claim. For examination purposes only, the phrases are taken to mean the following: (a) the phrase "biological activity" is deleted from the claim, (b) the phrase "histidine phosphatase" is

assumed to be "histidine protein phosphatase"; (c) "molecular weight of 13.000-15.000" is assumed to be molecular weight of 13-15 kDa determined by any method; (d) "affinity chromatography" is taken to mean any affinity column including reverse phase and hydrophobic columns, (e) the nucleic and amino acid sequences in claims 2, 3, 5, and 9 are assumed to be SEQ ID NO: 3, 5, 5, 2 and 1, respectively.

(b) The term "high specificity for phosphohistidine" in claims 1, 5 and 6 is a relative term which renders the claim indefinite. The term "high specificity" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Also, it is not clear whether the applicant are referring to a protein comprising a phosphorylated histidine residue or the amino acid histidine phosphorylated at the α-amino group, carboxyl group or one of the ring nitrogen. For examination purposes only, the phrase is taken to mean "binds to any phosphohistidine" derivative.

(c) claims 8, 10 and 11 are included in this rejection because they are dependent on a rejected claim and do not cure its deficiencies.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8 and 9 are rejected under 35 U.S.C. § 102(b) as being anticipated by Hillier *et al.* (IDS: reference AU).

Hillier *et al.* teach a nucleic acid fragment comprising the nucleic acid sequence of SEQ ID NO: 1, see the entire reference.

Allowable subject matter:

Claims directed to the human histidine protein phosphatase of SEQ ID NO: 2, a composition of said phosphatase, a recombinant method to make said phosphatase, and an antibody specific for the said phosphatase would be allowable over the prior art of record.

The following is a statement of reasons for the indication of allowable subject matter: The human histidine protein phosphatase of SEQ ID NO: 2 is not taught or suggested by the prior art of record.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is (703) 305-6586. The examiner can normally be reached Monday, Tuesday, Thursday, and Friday from 9:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (703) 308-3804. The fax phone numbers for this Group are (703) 305-3014 and (703)308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nashaat T. Nashed, Ph. D.
Primary Examiner